

In considering the use of the acne vaccine treatment several facts appear evident. First, that the results obtained with the polyvalent acne stock were fully as satisfactory as those obtained with an autogenous vaccine, also that much more depended on a careful oversight of the case, from the clinical standpoint, regulation of the amount and frequency of dosage and general hygienic care of patients, than on the fact that the vaccines were autogenous. This, of course, is of great advantage in the employment of the injection treatment, for the acne bacillus is at best a slow grower and requires considerable time and care.

Another fact observed is that old emulsions produce a more rapid immunity with less danger of local reaction or anaphylaxis than those freshly prepared. Any emulsion carefully prepared keeps indefinitely if care is taken to prevent contamination. This fact has also been observed in vaccine injections against typhoid, in which it has been shown that an old emulsion produces slight if any, constitutional reaction, as compared with fresh cultures.

A FATAL CASE OF TETANY WITH AUTOPSY FINDINGS SHOWING HEMORRHAGES IN THE PARATHYROID GLANDS.

By F. PROESCHER, M.D.,

PATHOLOGIST TO THE ALLEGHENY GENERAL HOSPITAL,

AND

THEODORE DILLER, M.D.,

NEUROLOGIST TO THE ALLEGHENY GENERAL HOSPITAL, PITTSBURG.

It is an acknowledged fact that tetany occurring after an operation for the removal of goitre is to be attributed to the removal of the parathyroid glands along with the thyroid gland, and that tetany of children is due to disease of the parathyroid glands.

Whether non-operative or spontaneous tetany occurring in adults is due to disease of the parathyroid glands or not is a question which is not yet settled. Indeed, as yet we have only insufficient data for deciding this question, as only few cases of fatal tetany in adults with postmortem findings have been recorded.

It has been our good fortune to observe a case of tetany in an adult in which the clinical course and postmortem findings seem to leave no doubt as to the diagnosis.

The parathyroid glands, which were discovered in 1880 by Sandstroem, were forgotten for ten years and again brought to our attention by the French physiologist Glay in 1891. The vital importance of the parathyroid glands is very generally recognized.

These glands are found on each side of the thyroid gland and sometimes embedded in the same. The number and position of these little glands show great individual variation. They are more numerous in children than in adults, and are bean-shaped, flat, and slightly translucent, of a yellow-brown color, and never lobulated. Oftentimes it is hard to distinguish them from fat tissue. Microscopically they consist of epithelial cells. Hence the name "epithelial bodies" given them by Kohn.¹

The cell masses are arranged in lobules or cell chains, between which a connective-tissue stroma runs which is less developed in younger individuals than in older ones. The bloodvessels are embedded in this stroma. The parenchyma consists of two different kinds of cells: The first are large polygonal and sharply outlined cells (cell type I), the protoplasm of which is colorless or slightly stained with eosin. Between these cells we find a deeper stained intercellular substance. The second type of cells are rich in chromatin (cell type II). They are indistinct in outline, and their scanty protoplasm is stained more or less with eosin. These cells are in some places closely packed together, giving the impression of being free nuclei. Koenigstein² has demonstrated on serial section that both types of cells are identical, and are different forms of the same cell, the differentiation having been produced by functional activity.

Petersen³ demonstrated with methyl-green pyronin stain that cell type I is a cell resting, while cell type II represents the cell in functional activity. The epithelial cells in young individuals contain much glycogen, and later fat drops. A few colloid drops may be found.

The colloid production found in the thyroid gland is not found in the parathyroid glands. In older individuals the glands are infiltrated with many large interstitial fat cells, which develop from the perivascular connective tissue.

The physiological function of the parathyroid glands became known to us only in the last few years. After overcoming many difficulties, Glay, who made the first experiments on rabbits, showed that the animals died of tetany after total extirpation of the thyroid glands with all the parathyroid glands. On extirpation of the thyroid gland without the parathyroid glands death did not occur. Glay believed that the parathyroid glands can perform the function of the thyroid gland, but on account of the irregular results from his experiments he could not give a clear idea of the function of the parathyroid glands.

Mousson took up Glay's experiments and criticised the same. He experimented on dogs, and reached the conclusion that the extirpation of the thyroid gland without the parathyroid glands

¹ (Collective references.) *Ergebn. d. Anat. Entwicklungsgesch.*, 1899, ix.

² *Wien. klin. Woch.*, 1906.

³ *Virchow's Arch.*, clxxiv, 1903.

does not cause tetany, but causes a chronic cachectic condition which the animal outlives. The extirpation of the parathyroid glands alone cause tetany, with fatal result.

This strict dualism of Mousson has been confirmed by a number of investigators: Vassale,⁴ Genralli, Walbum, Pineless,⁵ Erdheim,⁶ Hagenbach, Iselin, and others. Therefore, two different diseases may be distinguished: tetany parathyreopriva and cachexia thyreopriva. The term tetany thyreopriva is misleading, and is only a collective name for undifferentiated diseases. Without going into details of further experiments on animals, we may compare these with our clinical experience with human beings. We know that after thyroidectomy on human beings, tetany is observed, and it is believed that this is due to the removal of the parathyroid glands. The experimental experience on animals has demonstrated the same.

Erdheim was the first to throw light on the subject of operative tetany after thyroidectomy. He examined in serial sections the throat organs of two individuals dying after thyroidectomy, and could not find any trace of the parathyroid glands. The remaining portion of the thyroid was sufficient, it seemed, to protect the individual from cachexia thyreopriva. The result of Erdheim's investigation is in accord with animal experiments. Since surgeons have learned to avoid removal of all the parathyroid glands, tetany is very rare after thyroidectomy. Absolute proof as to the different functions of the parathyroid glands and the thyroid gland is seen in cases of so-called athyroidismus, or complete congenital defect of the thyroid. Here we have the typical picture of cretinism. In the cases which came to autopsy the parathyroid glands were found, but there was no trace of the thyroid gland. Experimental experience and the clinical observations are in harmony, and all argument against the functional activity of the parathyroid glands can now be disregarded.

We now approach the important and, to us, the most interesting question of the relationship of idiopathic, infantile, and adult tetany.

Erdheim was the first to discover hemorrhages in the parathyroid glands in cases of infantile tetany.

Yanase⁷ was the first to study this subject extensively, which he did from the cases in Escherich's clinic. He examined the parathyroid glands of 89 children coming to autopsy without any

⁴ Rivista experim. di freniatr., 1897; Arch. ital. de Biol., 1898; Münch. med. Woch., 1906, Nr. 33.

⁵ Sitzungsber d. Kais. Akad. d. Wiss. in Wien, 1903, Abt. iv; Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1904; Arb. a. d. Wien. Neurol. Inst., Nr. 16; Arch. f. klin. Med., lxxxv, 1906.

⁶ Wien. klin. Woch., 1901, Nr. 41; Zeit. f. Heilk., Abt. f. path. Anat., 1904; Mitt. a. d. Grenzgeb., 1906, xvi; Ziegler's Beitr., 1903, xxxiii; Sitzungsber. d. Wien. Akad. d. Wiss., 1907, Abt. iii (mathemat.-naturwissensch.).

⁷ Jahrb. f. Kinderheilk., lxxvii, 1908.

selection, ranging from birth to the fifteenth year. He found hemorrhages or remains of them in 33 children. In all, he examined 104 parathyroid glands and found 71 with hemorrhages. Therefore, hemorrhages in parathyroid glands are of frequent occurrence.

Yanase made systematic investigations of the electrical irritability in sick children, and at death he examined the parathyroid glands in 50 cases which came to autopsy; 30 of these showed a normal electrical irritability. At autopsy of these 30 cases the parathyroid glands were found normal, and no hemorrhages were found. In contrast, he found increased anodal electrical irritability in 22 children; and in 12 (55 per cent.) of these, hemorrhages were found in the parathyroid glands. Of 9 children under one year of age hemorrhages were found in each case. In the other 13 all of whom were older than one year, only 3 showed remnants of hemorrhages. Yanase came to the conclusion that in the remaining 10, hemorrhages had occurred which could not be found at the time of autopsy.

The latest investigations of Haberfeld⁸ has thrown some light on such cases of infantile tetany where no hemorrhages were found at autopsy. He found in these cases more or less marked atrophy, with or without remnants of hemorrhages, such as pigment or cyst formation. His thorough histological examination of these parathyroid glands has shown that hemorrhages not only destroy the histological structure, but also inhibit the development of the parathyroid glands and lead to a hypoplasia.

The reason that no symptoms of tetany were observed at the time of hemorrhage which generally occurs at time of birth is explained by Escherich,⁹ that the central nervous system of the newborn is insensitive to tetany toxin. The susceptibility to tetany begins about the third month. This theory seems to be supported by Quest,¹⁰ who found that the brain of the fetus contains the greatest amount of calcium, which decreases with the age of the child, and the irritability of the brain is increased with the decrease of calcium.

The opinion of Escherich and Quest is in accordance with the recent investigations of Voetglin and McCallum,¹¹ who revealed the fact that the calcium excretion of parathyroidectomized animals was increased and the tetany attacks could be eliminated by calcium salts injection.

Therefore, we conclude that infantile tetany is due to insufficiency of the parathyroid glands produced by hemorrhages.

Before discussion of the adult tetany we wish to report our case, that of a man, aged twenty-six years, a Russian, speaking little English, a butcher by occupation. He was admitted to the Allegheny General Hospital, May 25, 1909, in the service of

⁸ Virchow's Arch., cciii, Heft 2.

¹⁰ Jahrb. f. Kinderheilk., 1905.

⁹ Die Tetanie der Kinder.

¹¹ Jour. Exper. Med., 1909, xi, No. 1.

Dr. McNaugher, to whom we are under obligation for permission to examine the patient and to make this report. One week after admission, and two weeks after the onset of the disease, the patient died.

He had never been sick before the present illness except with an attack of influenza. His employer reports that he drank large quantities of pure alcohol and smoked cigarettes excessively. There was no history or sign of an infected wound.

Two weeks before admission the patient fell off a porch, a distance of five feet, and sustained an injury to the spine in the region of the third or fourth lumbar vertebrae. One week after this accident (two weeks before his death) he developed the first symptom of his fatal illness, an attack of rigidity in the arms and legs. These attacks came with increasing frequency and severity. When he was admitted to the hospital the attacks of rigidity affected the arms, legs, and trunk, including the neck. These attacks were intermittent and accompanied by considerable pain in the arms and legs, especially the latter. On admission, he complained much of pain in his legs. He asked to have his knees flexed, as he said this afforded great relief. It was noted that the patient became quite cyanotic during spasms, and that he perspired profusely.

May. 25. Sputum was negative for tubercle bacilli. The urine showed a slight trace of albumin and some hyaline casts.

May 28. Lumbar puncture was made, but resulted in a dry tap. The Wassermann test was negative.

Blood: Hemoglobin, 75 per cent.; red blood cells, 4,100,000; leukocytes, 7600. Differential count: Polynuclear neutrophiles, 78 per cent.; large lymphocytes, 11 per cent.; small lymphocytes, 10 per cent.; monocytes, 1 per cent.

On May 28 the patient was examined by Dr. Diller. The patient's mental condition seemed clear. Handling the arms and legs produced generalized spasms, which kept up for a minute or two. Pressure on the legs, even light pressure, caused a generalized spasm affecting the arms, legs, and trunk, and neck muscles. His position became one of opisthotonos; arms and legs were hyperextended. The legs were more involved than the arms. There were no spasms of the fingers and toes, and none of the face muscles; but pressure over the seventh nerve produced facial spasm. The masseters (especially examined) were free from spasms. Kneejerks were slightly increased; there were no Babinski signs.

The same day the eye-grounds were examined by Dr. A. C. Blair and found to be normal. The nurse noted that the spasms came particularly when the patient attempted to raise his knees; and in his examination, Dr. Diller noted the same. The spasms now came spontaneously without handling of the limbs, but they were especially provoked by handling or pressure anywhere on the legs or arms, especially the former.

On June 1 the patient was again examined by Dr. Diller. Prior to this his temperature had been normal, but his pulse had been accelerated, ranging from 90 to 120. On this day his temperature suddenly shot up to 103°, and he died a few hours later. For the preceding three days he had had no spasms in the daytime, but they were especially severe at night. At this examination no spasms were produced by pressure of the arms and legs, even when made over the vessels and nerves, but there was resistance in both arms and legs to passive movements. There were no spasms of the masseters, but considerable stiffness of the neck muscles.

The patient died a few hours after this examination was made.

The autopsy showed an external fibrous pachymeningitis, chronic leptomeningitis, edema, and hyperemia of the brain, hyperemia of the spinal cord, bilateral adhesive pleuritis, spleen slightly enlarged, hemorrhagic gastro-enteritis, hyperemia of kidney and liver, with slight parenchymatous cloudiness.

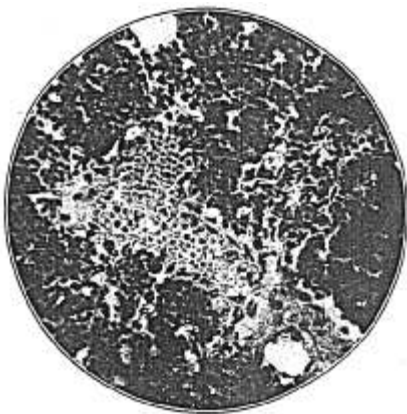


FIG. 1.—Ruptured bloodvessel with perivascular hemorrhage. Leitz, objective 5; ocular 4.

Special attention was given to the examination of the parathyroid glands; which in this case were found without any difficulty. Two were on the right side and one on the left side. The two former measured 10 mm. long by 3 mm. broad, and 9 mm. long by 2.5 mm. broad, while that on the left side measured 11 mm. by 3 mm. broad. Macroscopically the glands were opaque and brownish in color, with red punctations having the appearance of hemorrhages. The symptoms of tetany could not be accounted for by

the macroscopic changes found at autopsy, except for the suspicion of hemorrhages of the parathyroid glands. The pachymeningitis, leptomenigitis, and gastro-enteritis were probably of alcoholic origin.

Microscopic Examination of the Organs. The changes in the three parathyroid glands were almost uniform. With low power, extensive infiltration of the parenchyma with large fat cells was noted, causing partial atrophy. The connective-tissue stroma was greatly thickened and divided the parenchyma into various sized lobules. Bloodvessels and capillaries were greatly distended. With higher power the parenchyma consisted largely of small, indistinctly outlined epithelial cells which were rich in chromatin

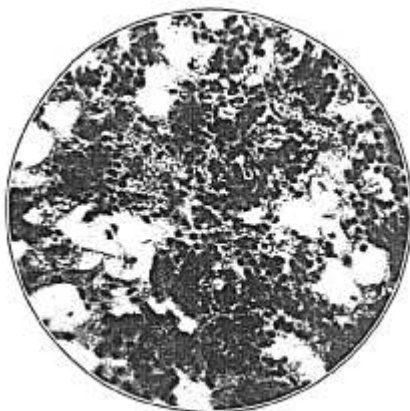


FIG. 2.—Parenchyma invaded by profuse hemorrhages. Leitz, objective 5; ocular 4.

(cell type II). The protoplasm stained bluish red. On the edge of the gland were found large, compact, distinctly outlined polygonal epithelial or oxyphile cells (cell type I). The protoplasm of these cells was finely granular, somewhat cloudy, and stained fairly well with eosin. The small intercellular mass stained more deeply with eosin. The nuclei of the cells were not so rich in chromatin as in cell type II, and as in some near the periphery. Some cells were without nuclei. Small groups of the same cells were found inside of cell type II.

The fine granulated appearance and the bluish-red color of cell type I and II suggested a slight parenchymatous degeneration. In

normal epithelial cells the protoplasm stains deep red with eosin, or is nearly colorless.



FIG. 3.—Same as Fig. 2. Leitz, objective 5; ocular 4.



FIG. 4.—Same as Fig. 1. Leitz, objective 5; ocular 4.

The most interesting morbid change in the glands was the multiple hemorrhages which were diffused throughout one-half to two-thirds of the parenchyma in the form of small circumscribed areas. These hemorrhages could be traced to medium-sized blood-vessels. Larger perivascular hemorrhages, as found in the parathyroid glands of children, were not noted. The appearance of the hemorrhages was as follows: The red blood cells lay directly on the epithelial cells, which could be demonstrated with the Van Gieson stain. In contrast with the distended bloodvessels and capillaries fine, spindle-shaped endothelial cells were seen, deeply stained and at regular distances apart, which differentiated them from a hemorrhage. The fibrous adventitia of the vessels showed slight hyaline degeneration. Some vessels had very small lumina. The walls of the veins were much distended. In some places drops of colloid inside of glandular-like formations of epithelial cells were seen.

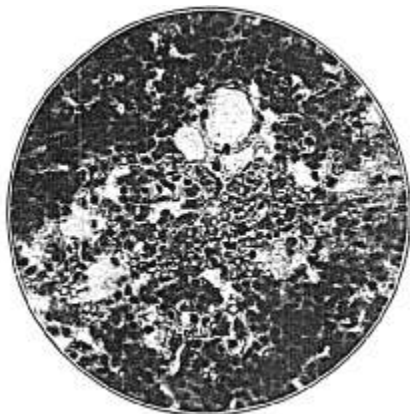


FIG. 5.—Same as Figs. 1 and 4. Leitz, objective 6; ocular 4.

Retrogressive changes of the hemorrhages, such as pigment, were not found, and this led to the conclusion that the hemorrhages must have been of recent origin.

The red blood cells presented a peculiar appearance. Some of them appeared deeply stained with eosin and were distinctly outlined. Others were merely visible and were stained very lightly. One received the impression that the hemoglobin had been extracted from them. We believe that this phenomenon is not due

to incomplete fixation. Petersen¹² has called our attention to this phenomenon. In his opinion the deeply stained bloodvessels are loaded with colloid, which is transported by the red cells through the organism. But we are not prepared to accept this view.

Microscopic Examination of the Central Nervous System. Numerous sections of the cortex and spinal cord, stained after Nissl, showed that the large pyramidal cells in the cortex were degenerated (absence of tigroid and vacuolation); some cells were without nuclei. The dendrites were greatly elongated. Practically the same change was found in the large cells of the anterior horns of the cord. No noteworthy change was seen in the white matter or the bloodvessels. The cells in the spinal ganglia were without change, and the peripheral nerves appeared normal.



FIG. 6.—Large pyramidal cells of cortex of the frontal lobe of brain, stained after Nissl, showing prolongation of dendrite and absence of tigroid. Leitz, $\frac{1}{2}$ oil immersion; ocular 4.

The kidney and liver showed slight parenchymatous cloudiness, and their bloodvessels were greatly distended. The mucous membrane of intestine and stomach showed a few small hemorrhages.

In addition to our case, we review briefly the cases of tetany adutorum which can be divided into three groups.

Group I. Four cases of Haberfeld,¹³ with typical clinical symptoms of tetany and changes of the parathyroid glands, found at autopsy. Case I showed amyloid degeneration of the small blood-

¹² Loc. cit.

¹³ Loc. cit.

vessels and cyst formation of the large polygonal cells. Cases II and III showed hypoplasia, with cicatrix due to previous disease. Case IV, the first case of tetany gravidarum studied, showed hypoplasia and cicatrix of the parathyroid glands. This group may be named "hypothyroidismus."

Group II. One case of McCallum,¹⁴ with typical clinical tetany, and no parathyroid glands found at autopsy (apathyroidismus).

Group III. Three cases of Erdheim,¹⁵ two of gastric tetany and one from brain tumor; one case of Koenigstein, carcinoma of the pancreas, all with typical clinical tetany, and no microscopic changes in the parathyroid glands.

The question arises as to whether any relation exists between tetany adutorum and the parathyroid glands. Cases under Group I and II are undoubtedly due to disease of the parathyroid glands. As above stated, the recent investigations of Habersfeld have proved atrophy of the parathyroid glands to be the chief cause of infantile tetany, and in all probability it is also the cause of tetany adutorum.

McCallum's case of apathyroidismus stands isolated, and its explanation is difficult. The apathyroidismus was either due to a congenital defect or a destructive lesion of the glands.

In our opinion it is not likely that it was due to a congenital defect, because the individual would not have lived so long without symptoms of tetany, but on account of their probable atrophic condition the parathyroids might have been overlooked. On the other hand, there might have been a lesion attended with complete destruction of the glands, thus causing tetany, or possibly there might have been an acquired serogen or histogen immunity to tetany toxin which has been demonstrated by animal experiments (Blum). Finally, the individual may have died from acute intoxication from tetany toxin, which could not be neutralized.

How may we account for the third group where no microscopic change of the parathyroid glands was found?

We believe that in such cases there was a hypoparathyroidismus due to atrophy of the gland without any other microscopic change.

The study of these cases was during the earliest investigations of the epithelial body, when the significance of the atrophy of the gland was not taken into consideration.

Our knowledge of the pathological anatomical changes in the parathyroid glands is limited. The latest investigations show that the parathyroid glands are very rarely diseased, at least we find in the literature very few observations of typical pathological changes.

Infiltration of the glands was found in leukemia, pernicious anemia, bacterial emboli with metastatic abscesses by Erdheim

¹⁴ Die Beziehung der parathyroiddrüsen zur Tetanie, Ztbl. f. allg. Path. u. path. Anat., lxxvi, 1905.

¹⁵ Loc. cit.

and Yanase; tubercular and syphilitic inflammation by Pepere,¹⁶ Benjamin, Schmorl,¹⁷ Koenigstein,¹⁸ Carnot and Derion,¹⁹ Verebely,²⁰ Stumme, Yanase; tumors, myoma, by Pepere; adenoma by De Lauti, Erdheim, Benjamin, and McCallum; lymphoma and angioma by Askanazy, Weichselbaum, and Verebely.

In all these cases these findings were accidental as no tetany was observed.

Hemorrhages in the parathyroid glands of adults without tetany were found by Erdheim in a man, aged forty-five years, who died of tuberculosis.

Pepere found hemorrhages in 2 cases: one, a girl, aged eighteen years, with a heart lesion and hemorrhages and cyst formation without pigment in one parathyroid gland; the other, a man, aged eighty-two years, without special clinical and anatomical findings, with fresh hemorrhages in one gland.

Verebely found rather recent hemorrhages in two glands, hema-togen pigment in surrounding tissue, in a man, aged thirty-eight years, the cause of death is not mentioned.

Our case is the first in which an adult with tetany and hemorrhages of all parathyroid glands was observed. We believe the hemorrhages were all of recent occurrence, because no pigment was present. All three glands showed more or less primary atrophy of the parenchyma, followed by hemorrhages, which we believe were the indirect cause of the tetany.

Here the already atrophic glands were rendered insufficient by the hemorrhages.

In the infantile tetany we have first the hemorrhages which produce the atrophy of the glands.

According to Haberfeld²¹ the diseased epithelial bodies are not alone responsible for the tetany, and a person could live for a long time with changed glands until disturbances, such as intestinal auto-intoxication, pregnancy, etc., would cause increased activity, which leads to tetany. Therefore, the insufficiency of the parathyroid glands is the chief cause of tetany.

He distinguishes between absolute and relative tetany. The absolute is derived from the absence of the epithelial body (operative tetany). The relative tetany is caused by increased metabolic products, which cannot be neutralized by the normal parathyroid glands or by a normal amount of metabolic products which cannot be neutralized by the insufficient parathyroid glands.

His latest investigations prove that changed parathyroid glands

¹⁶ Leghiandole paratiroida. Turin 1906; Arch. d. Anat. e di Embriol., viii, fasc. 2, 1909; Arch. de m d. exp r., January, 1908.

¹⁷ M nch. med. Woch., 1907.

¹⁸ Ges. f. inn. Med. u. Kinderheilk., December 6, 1906.

¹⁹ Compt. rend. dela Soc. de Biol., 1905.

²⁰ Virchow's Arch., 1907, clxxvii.

²¹ Die Epithelk rperchen bei Tetanie und bei einigen anderen Erkrankungen, Virchow's Arch., cciii, Heft 2.

plus increased metabolic activity is the chief factor in producing tetany, and "in infantile tetany this seems to be a law."

The disturbances are also the predisposing cause, the exciting cause being of unknown source.

Some investigators, especially Koenigstein, claim that the microscopic change in the gland is not sufficient to account for the clinical symptoms of tetany, but this opinion cannot be accepted.

All variations of the pathological process in the parathyroid gland lead to disturbance or decrease in their function.

A few referred diseases²² of the parathyroid glands are not recognized by Erdheim and Haberfeld.

The hyperplasia of the gland found by Erdheim in osteomalacia remains to be studied. At present we can only say the diseased parathyroid glands cause tetany; as to other diseases, nothing has been demonstrated.

The real etiology of tetany is unknown, but it seems to be of an enterogenous origin. Without doubt the glands have the functions to avert and deintoxicate certain toxic products (autoneurotoxins), which are formed during metabolism, and which have a great affinity for the central nervous system. They also play the role of a protective apparatus for the central nervous system.

The clinical observation and pathological examination in conjunction with animal experiments have solved one of the most difficult problems of the ductless glands, and it is hoped that the real etiology of the tetania parathyreopriva will soon be made clear.

RHEUMATIC MYOSITIS.

By V. C. ROWLAND, M.D.,

CLEVELAND, OHIO.

(From the medical Dispensary of the Lakeside Hospital, Cleveland.)

THE particular phase of the large subject of muscular rheumatism considered in this paper is the relation of certain acute inflammatory conditions of the muscles to acute rheumatic fever. Chronic muscular rheumatism was fully described so long ago as 1816 by Balfour. Rheumatic involvement of muscles was also extensively studied by the Swedes, notably by Froriep, in 1843, and Helleday, in 1876. They, however, paid more attention to the chronic nodular condition and its treatment by massage. Considerable was written about the subject of acute myositis in the

²² *Eclampsia gravidarum* (Vassale Zanfognini), *paralysis agitans* (Lundborg), *myasthenia gravis pseudoparalytica* (Lundborg and Chrostek).